

### **REMARKS**

Claims 12-14, 16-22, 26-29 and 33-38 are pending. The amendment to claims 12, 26 and 33 is supported in the originally filed specification at least at p.29, lines 10-11, Experiment 1. No new matter is added.

The Applicant appreciates that the previously filed Declaration is sufficient to overcome the previous rejection of the claims based upon Soma, as evidenced by Inagawa.

**Claims 12, 14, 16-19, 26, 28, 33, and 35 are newly rejected under 35 USC § 102 (b) as being anticipated by Mulyowidarso et al (Mulyowidarso et al, The microbial ecology of soybean soaking for tempe production, International Journal of Food Microbiology, 8 (1989) 35-46), as evidenced by Inagawa et al (Homeostasis as regulated by activated macrophage. II. LPS of plant origin other than wheat flour and their concomitant bacteria, Chem. Pharm. Bull. 40 (4) 994-997, 1992). (Office Action, page 3)**

Mulyowidarso et al. teach soybean tempe is a fermented food. *Lactobacillus casei*, *Streptococcus faecium*, *Staphylococcus epidermidis* and *Streptococcus dysgalactiae* dominated the fermentation but, significant contributions were also made by *Klebsiella pneumoniae*, *Klebsiella ozaenae*, *Enterobacter cloacae*, *Enterobacter agglomerans*. The article shows that a strong microbial fermentation of complex ecology develops soaking of soybeans. Several species of bacteria and yeast were identified in the complex ecology, as shown in Table 1 of the article.

However the claimed invention has the critical step of “simultaneously culturing solely said facultative anaerobic gram-negative bacterium in a medium containing no component derived from an animal” which is not suggested by the complex ecology of bacteria or yeast on any plant source. Example 1 of the published specification is illustrative:

#### **A. EXAMPLES RELATING TO METHOD FOR PRODUCING FERMENTED WHEAT EXTRACT**

##### **Example 1**

##### **Growth Study of *Pantoea agglomerans* in Wheat Flour Medium**

[0080] In order to confirm whether *Pantoea agglomerans* which is the indigenous

symbiotic bacterium with wheat can grow using the wheat flour as the carbon source, the growth of *Pantoea agglomerans* in a wheat flour solid medium was examined.

[0081] (1) M9 agar medium containing 0.5% wheat flour as the carbon source was made.

[0082] (2) *One colony of Pantoea agglomerans was picked up from the LB agar medium, and suspended in 1 ml of PBS.* This was sequentially diluted 10 times to 10,000 times, and 0.1 ml of each aliquot was seeded on the M9 agar medium of (1).

[0083] (3) *After culturing at 37°C for 6 days, appearance of colonies was observed.* As a result, about 300 colonies were observed in a petri dish in which 0.1 ml of the dilution 10,000 times had been seeded.

[0084] This has confirmed that *Pantoea agglomerans* can utilize wheat flour as the carbon source.

The invention is the simultaneous culturing of a specific bacterium, in addition to other method steps. This isolated step is not suggested by a complex ecology as studied in Mulyowidarso et al. and noted in Inagawa. Thus the combination of references do not make obvious the method as claimed which focuses on a specific bacterium.

Without more, Mulyowidarso et al. and Inagawa do not make the invention now clarified *prima facie* obvious. Thus, it is respectfully requested that the rejection be reconsidered and withdrawn.

**Claims 12-14, 16-22, 26-29, and 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mulyowidarso et al and Inagawa et al as applied to claims 12, 14, 16-19, 26, 28, 33, and 35 above, and further in view of Matsuo et al (Matsuo et al, Suppression of plasma cholesterol elevation by Okara tempe in rats, Biosci Biotech Biochem 57 (7): 1188-1190, 1993). (Office Action, page 5)**

Mulyowidarso et al disclose soybean is fermented by many microorganisms. It is *Lactobacillus casei*, *Streptococcus faecium*, *Staphylococcus epidermidis* and *Streptococcus dysgalactiae* that dominate the fermentation. *Klebsiella pneumoniae*, *Klebsiella ozaenae*, *Enterobacter cloacae* and *Enterobacter agglomerans* only contribute to the fermentation. In particular, *Streptococcus dysgalactiae* is known for decomposing starch.

Vieira et al (Veronica V. Vieira et al, "Genetic relationships among the different phenotypes of *Streptococcus dysgalactiae* strains" International Journal of Systematic Bacteriology (1998), 48, pp.1231-1243) page 1235 right column item "RESULTS" lines 1 to 4 reads "All strains of *S. dysgalactiae* sub-groups were positive for acid production from ... starch ..." This means *Streptococcus dysgalactiae* decomposes starch.

The attached pathway shows *Streptococcus dysgalactiae* decomposes starch into Glycogen, Amylose, Dextrin and  $\alpha$ -D-Glucose. (Right hand lower part shows "Starch" and the darker squares are enzymes.)

Furthermore, *Pantoea agglomerans* was not known for being able to decompose starch as explained in the present published specification [0004] (emphasis added).

[0004] Meanwhile, when the fermentation is performed by the bacteria, generally there are nutrient conditions which a fermentation substrate should meet for bacteria growth. That is, the presence of substances available as nutrients by the bacteria is essential, i.e., monosaccharides such as glucose and fructose as carbon sources are sufficiently contained. Therefore, fruits such as grapes containing abundant fructose can be utilized as the fermentation substrate without giving any processing. However, in other cases, a pretreatment such as heating and enzyme treatment for the fermentation by the bacteria is required. For example, the foregoing *Zymomonas mobilis* is a bacterium used for the tequila fermentation. In this case, polysaccharides obtained from the rootstocks of the maguey which is not edible plant are decomposed into fermentable monosaccharides by heating, and subsequently the monosaccharides are fermented by the bacteria to yield the alcohol as the fermentation product. Therefore, when the fermentation culture is performed using a typical bacterium, the polysaccharides such as starch are not suitable as the fermentation substrate. ***For example, it has been described that *Pantoea agglomerans* cannot decompose starch (Non-patent document 4).***

Both Mulyowidarso et al. and Matsuo fail to disclose culturing solely a specified bacterium equivalent to *Pantoea agglomerans* in a specified circumstance. The claimed invention is to aim at an immunopotentiator obtained inexpensively and efficiently using safe materials as explained in the present published specification [0035].

[0035] In the light of the above problems, the present invention aims at providing a method for fermentation and culture in which an immunopotentiator can be obtained inexpensively and efficiently using safe materials, a fermented plant extract obtained by the method, fermented plant extract powder obtained from the fermented plant extract and a fermented plant extract composition containing the fermented plant extract powder.

In light of the fact that the combination of cited art fails to culturing solely a specified bacterium equivalent to *Pantoea agglomerans*, the combination cannot make a *prima facie* rejection of obviousness. It is respectfully requested that the rejection be reconsidered and withdrawn.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105.

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Respectfully submitted,

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Attachments: Starch and Sucrose Pathway (1 page).